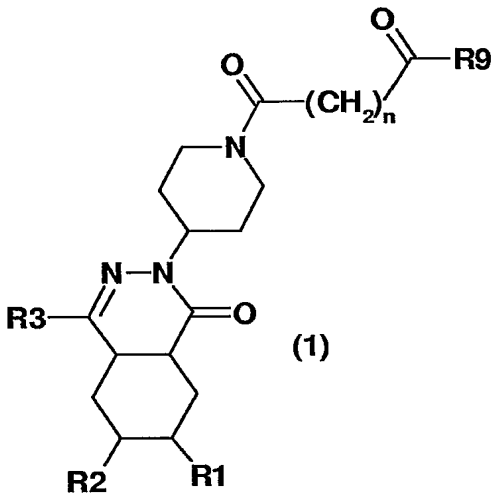
Patent claims

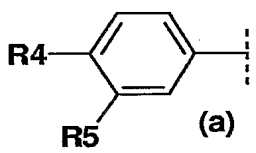
1. Compounds of formula 1

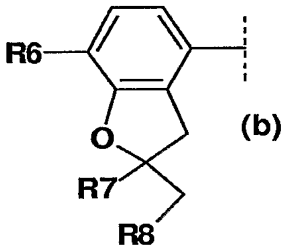


in which

R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a phenyl derivative of formulae (a) or (b)





wherein

R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is 1-4C-alkyl and

R8 is hydrogen or 1-4C-alkyl,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

R9 is hydroxyl, 1-4C-alkoxy, -N(R10)H, -N(H)N(R11)R12 or -N(R13)R14,

R10 is hydroxyl, 1-4C-alkoxy or 1-4C-alkoxy-2-4C-alkyl,

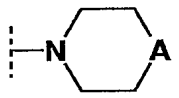
R11 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

R12 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

R13 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

R14 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

or R13 and R14 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-hexahydroazepinyl-ring or a ring of formula (c),



(c)

wherein

A is O, S, SO, SO_2 or NR15,

R15 is hydrogen, 1-4C-alkyl, phenyl, pyridyl, $-(CH_2)_m$-R16 or $-(CH_2)_p$-C(O)R17,

R16 is -N(R18)R19,

R17 is -N(R20)R21,

R18 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

R19 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

or R18 and R19 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-piperazinyl, 1-(1-4C-alkyl)-piperazin-4-yl-, 1-hexahydroazepinyl-, 4-morpholinyl-, 4-thiomorpholinyl-, thiomorpholin-1-oxide-4-yl- or thiomorpholin-1,1-dioxide-4-yl-ring,

R20 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

R21 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

or R20 and R21 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-piperazinyl, 1-(1-4C-alkyl)-piperazin-4-yl-, 1-hexahydroazepinyl-, 4-morpholinyl, 4-thiomorpholinyl-, thiomorpholin-1-oxide-4-yl- or thiomorpholin-1,1-dioxide-4-yl-ring,

n is 0, 2, 3 or 4,

m is 2, 3 or 4,

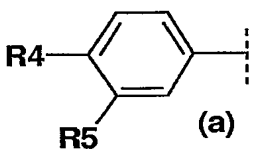
p is 1, 2, 3 or 4,

and the salts of these compounds.

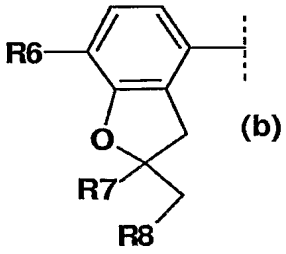
2. Compounds of formula 1 according to claim 1, in which

R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a phenyl derivative of formulae (a) or (b)



(a)



(b)

wherein

R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is 1-4C-alkyl and

R8 is hydrogen or 1-4C-alkyl,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

R9 is 1-4C-alkoxy, -N(R10)H, -N(H)N(R11)R12 or -N(R13)R14,

R10 is hydroxyl, 1-4C-alkoxy or 1-4C-alkoxy-2-4C-alkyl,

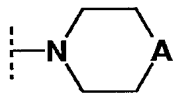
R11 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

R12 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

R13 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

R14 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

or R13 and R14 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-hexahydroazepinyl-ring or a ring of formula (c),



(c)

wherein

A is O, S, SO, SO_2 or NR15,

R15 is hydrogen, 1-4C-alkyl, phenyl, pyridyl, $-(CH_2)_m$-R16 or $-(CH_2)_p$-C(O)R17,

R16 is -N(R18)R19,

R17 is -N(R20)R21,

R18 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

R19 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

or R18 and R19 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-piperazinyl, 1-(1-4C-alkyl)-piperazin-4-yl-, 1-hexahydroazepinyl-, 4-morpholinyl-, 4-thiomorpholinyl-, thiomorpholin-1-oxide-4-yl- or thiomorpholin-1,1-dioxide-4-yl-ring,

R20 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

R21 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

or R20 and R21 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-piperazinyl, 1-(1-4C-alkyl)-piperazin-4-yl-, 1-hexahydroazepinyl-, 4-morpholinyl, 4-thiomorpholinyl-, thiomorpholin-1-oxide-4-yl- or thiomorpholin-1,1-dioxide-4-yl-ring,

n is 0, 2, 3 or 4,

m is 2, 3 or 4,

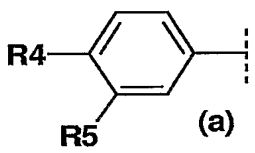
p is 1, 2, 3 or 4,

and the salts of these compounds.

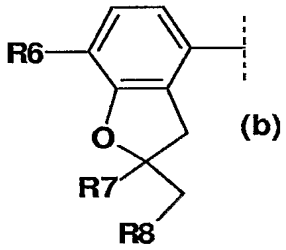
3. Compounds of formula 1 according to claim 1, in which

R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a phenyl derivative of formulae (a) or (b)



(a)



(b)

wherein

R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is 1-4C-alkyl and

R8 is hydrogen or 1-4C-alkyl,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

R9 is 1-4C-alkoxy, -N(R10)H, -N(H)N(R11)R12 or -N(R13)R14,

R10 is hydroxyl, 1-4C-alkoxy or 1-4C-alkoxy-2-4C-alkyl,

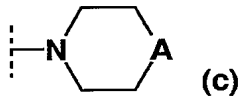
R11 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

R12 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

R13 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

R14 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

or R13 and R14 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-hexahydroazepinyl-ring or a ring of formula (c),



(c)

wherein

A is O, S, SO, SO_2 or NR15,

R15 is hydrogen, 1-4C-alkyl, phenyl, pyridyl, $-(CH_2)_m$-R16 or $-(CH_2)_p$-C(O)R17,

R16 is -N(R18)R19,

R17 is -N(R20)R21,

R18 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

R19 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

or R18 and R19 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-piperazinyl, 1-(1-4C-alkyl)-piperazin-4-yl-, 1-hexahydroazepinyl-, 4-morpholinyl-, 4-thiomorpholinyl-, thiomorpholin-1-oxide-4-yl- or thiomorpholin-1,1-dioxide-4-yl-ring,

R20 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

R21 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

or R20 and R21 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-piperazinyl, 1-(1-4C-alkyl)-piperazin-4-yl-, 1-hexahydroazepinyl-, 4-morpholinyl, 4-thiomorpholinyl-, thiomorpholin-1-oxide-4-yl- or thiomorpholin-1,1-dioxide-4-yl-ring,

n is 2, 3 or 4,

m is 2, 3 or 4,

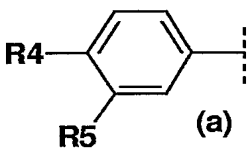
p is 1, 2, 3 or 4,

and the salts of these compounds.

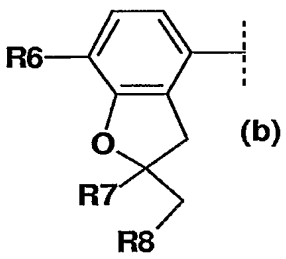
4. Compounds of formula 1 according to claim 1, in which

R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a phenyl derivative of formulae (a) or (b)



(a)



(b)

wherein

R4 is 1-2C-alkoxy or 1-2C-alkoxy which is completely or predominantly substituted by fluorine,

R5 is 1-4C-alkoxy,

R6 is 1-2C-alkoxy or 1-2C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is methyl and

R8 is hydrogen,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked cyclopentane, cyclohexane, tetrahydrofuran or tetrahydropyran ring,

R9 is -N(R10)H, -N(H)N(R11)R12 or -N(R13)R14,

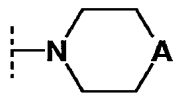
R10 is hydroxyl or 1-4C-alkoxy,

R11 is hydrogen or 1-4C-alkyl,

R12 is hydrogen or 1-4C-alkyl,

R13 and R14 are identical and are hydrogen or 1-4C-alkyl,

or R13 and R14 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-hexahydroazepinyl-ring or a ring of formula (c),



(c)

wherein

A is O, S or NR15,

R15 is hydrogen, 1-4C-alkyl or -$(CH_2)_p$-C(O)R17,

R17 is -N(R20)R21,

R20 is hydrogen or 1-4C-alkyl,

R21 is hydrogen or 1-4C-alkyl,

or R20 and R21 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-piperazinyl, 1-(1-4C-alkyl)-piperazin-4-yl-, 1-hexahydroazepinyl-, 4-morpholinyl or 4-thiomorpholinyl-ring,

n is 2,

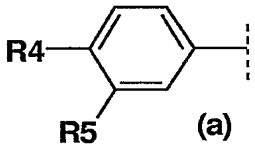
p is 1,

and the salts of these compounds.

5. Compounds of formula 1 according to claim 1, in which

R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a phenyl derivative of formula (a)



wherein

R4 is methoxy or ethoxy,

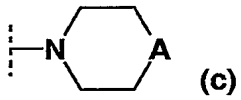
R5 is methoxy or ethoxy,

R9 is –N(R13)R14,

R13 is hydrogen,

R14 is hydrogen,

or R13 and R14 together and with inclusion of the nitrogen atom to which they are bonded, form a ring of formula (c),



wherein

A is O or NR15,

R15 is methyl or -$(CH_2)_p$-C(O)R17,

R17 is 1-pyrrolidinyl,

n is 2,

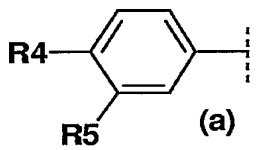
p is 1,

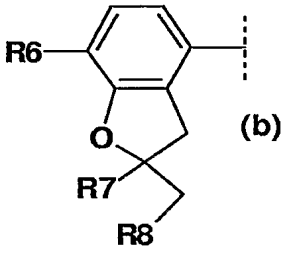
and the salts of these compounds.

6. Compounds of formula 1 according to claim 1, in which

R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a phenyl derivative of formulae (a) or (b)





wherein

R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is 1-4C-alkyl and

R8 is hydrogen or 1-4C-alkyl,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

R9 is hydroxyl, 1-4C-alkoxy, -N(R10)H, -N(H)N(R11)R12 or -N(R13)R14,

R10 is hydroxyl, 1-4C-alkoxy or 1-4C-alkoxy-2-4C-alkyl,

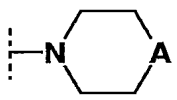
R11 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

R12 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

R13 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

R14 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

or R13 and R14 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-hexahydroazepinyl-ring or a ring of formula (c),



(c)

wherein

A is O, S, SO, SO_2 or NR15,

R15 is hydrogen, 1-4C-alkyl, phenyl, pyridyl, $-(CH_2)_m$-R16 or $-(CH_2)_p$-C(O)R17,

R16 is -N(R18)R19,

R17 is -N(R20)R21,

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or R18 and R19 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-piperazinyl, 1-(1-4C-alkyl)-piperazin-4-yl-, 1-hexahydroazepinyl-, 4-morpholinyl-, 4-thiomorpholinyl-, thiomorpholin-1-oxide-4-yl- or thiomorpholin-1,1-dioxide-4-yl-ring,

R20 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

R21 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkylmethyl,

or R20 and R21 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-piperazinyl, 1-(1-4C-alkyl)-piperazin-4-yl-, 1-hexahydroazepinyl-, 4-morpholinyl, 4-thiomorpholinyl-, thiomorpholin-1-oxide-4-yl- or thiomorpholin-1,1-dioxide-4-yl-ring,

n is 0,

m is 2, 3 or 4,

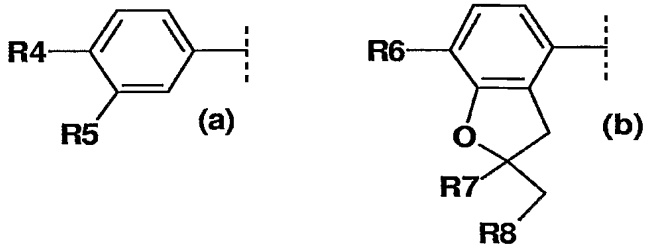
p is 1, 2, 3 or 4,

and the salts of these compounds.

7. Compounds of formula 1 according to claim 1, in which

R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a phenyl derivative of formulae (a) or (b)



wherein

R4 is 1-2C-alkoxy or 1-2C-alkoxy which is completely or predominantly substituted by fluorine,

R5 is 1-4C-alkoxy,

R6 is 1-2C-alkoxy or 1-2C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is methyl and

R8 is hydrogen,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked cyclopentane, cyclohexane, tetrahydrofuran or tetrahydropyran ring,

R9 is -N(R10)H, -N(H)N(R11)R12 or -N(R13)R14,

R10 is hydroxyl, 1-4C-alkoxy or 1-4C-alkoxy-2-4C-alkyl,

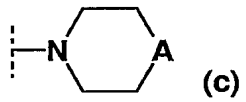
R11 is hydrogen or 1-4C-alkyl,

R12 is hydrogen or 1-4C-alkyl,

R13 is hydrogen or 1-4C-alkyl,

R14 is hydrogen or 1-4C-alkyl,

or R13 and R14 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-hexahydroazepinyl-ring or a ring of formula (c),



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or R20 and R21 together and with inclusion of the nitrogen atom to which they are bonded, form a 1-pyrrolidinyl-, 1-piperidinyl-, 1-piperazinyl, 1-(1-4C-alkyl)-piperazin-4-yl-, 1-hexahydroazepinyl-, 4-morpholinyl or 4-thiomorpholinyl-ring,

n is 0,

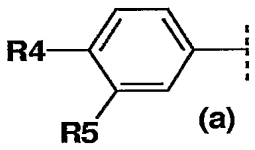
p is 1,

and the salts of these compounds.

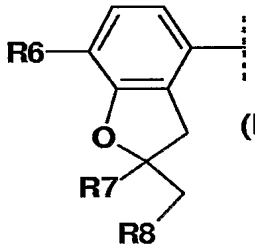
8. Compounds of formula 1 according to claim 1, in which

R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a phenyl derivative of formulae (a) or (b)



(a)



(b)

wherein

R4 is methoxy or ethoxy,

R5 is methoxy or ethoxy,

R6 is methoxy,

R7 is methyl and

R8 is hydrogen,

R9 is -N(R10)H, -N(H)N(R11)R12 or -N(R13)R14,

R10 is hydroxyl or methoxyethyl,

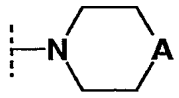
R11 is methyl,

R12 is methyl,

R13 is hydrogen or methyl,

R14 is hydrogen or methyl,

or R13 and R14 together and with inclusion of the nitrogen atom to which they are bonded, form a ring of formula (c),



(c)

wherein

A is O or NR15,

R15 is methyl,

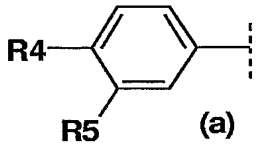
n is 0,

and the salts of these compounds.

9. Compounds of formula 1 according to claim 1, in which

R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a phenyl derivative of formula (a)



wherein

R4 is methoxy or ethoxy,

R5 is methoxy or ethoxy,

R9 is -N(R10)H, -N(H)N(R11)R12 or -N(R13)R14,

R10 is hydroxyl or methoxyethyl,

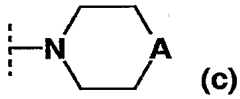
R11 is methyl,

R12 is methyl,

R13 is hydrogen or methyl,

R14 is hydrogen or methyl,

or R13 and R14 together and with inclusion of the nitrogen atom to which they are bonded, form a ring of formula (c),



wherein

A is O or NR15,

R15 is methyl,

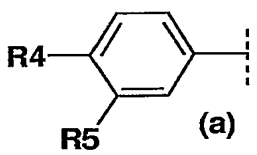
n is 0,

and the salts of these compounds.

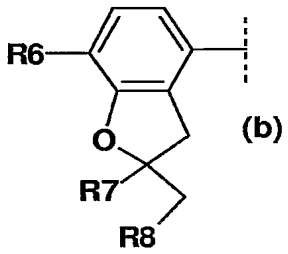
10. Compounds of formula 1 according to claim 1, in which

R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a phenyl derivative of formulae (a) or (b)



(a)



(b)

wherein

R4 is methoxy or ethoxy,

R5 is methoxy or ethoxy,

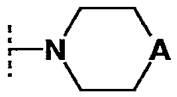
R6 is methoxy,

R7 is methyl and

R8 is hydrogen,

R9 is -N(R13)R14,

R13 and R14 together and with inclusion of the nitrogen atom to which they are bonded, form a ring of formula (c),



(c)

wherein

A is O,

n is 0,

and the salts of these compounds.

11. Compounds of formula 1 according to any of the claims 1 to 10, in which the absolute configuration (according to the rules of Cahn, Ingold and Prelog) is S in the position 4a and R in the position 8a.

12. Compounds of formula 1 according to claim 1 for use in the treatment of diseases.

13. Pharmaceutical compositions containing one or more compounds of formula 1 according to claim 1 together with the usual pharmaceutical auxiliaries and/or carrier materials.

14. Use of compounds of formula 1 according to claim 1 for the preparation of pharmaceutical compositions for the treatment of airway disorders.

15. A method for treating an illness treatable by the administration of a PDE4 inhibitor in a patient comprising administering to said patient in need thereof a therapeutically effective amount of a compound of formula 1 as claimed in claim 1.

16. A method for treating airway disorders in a patient comprising administering to said patient a therapeutically effective amount of a compound of formula 1 as claimed in claim 1.